

ATTACHMENT D.

**STUDY PROCEDURE: DETERMINATION OF AMERICAN FERTILITY
SOCIETY ADHESION SCORE IN INTERGEL® SOLUTION PIVOTAL TRIAL**

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The primary effectiveness variable in the amendment to the INTERGEL® Solution pivotal trial was evaluation of adnexal adhesions, using the Adhesion Scoring Method of the American Fertility Society (AFS 1988). Adhesions occurring at each of the adnexal adhesion sites were assessed for severity and extent by the investigators performing the surgery. The adnexal sites scored reflect observations at 4 regions as shown in Table 1 below:

Table 1
ANATOMICAL REGIONS INCLUDED IN AFS SCORE

Adnexa	Region	Site #	Anatomical Site
Right Adnexa	Right Ovary	15	Right ovary- lateral aspect
		16	Right ovary- medial aspect
		17	Right ovarian fossa
	Right Tube	21	Right tube
		22	Right ampulla
Left Adnexa	Left Ovary	18	Left ovary- lateral aspect
		19	Left ovary- medial aspect
		20	Left ovarian fossa
	Left Tube	23	Left tube
		24	Left ampulla

Each of the 10 anatomical sites was assessed for both severity and extent of adhesions. A severity grade was assigned to each of the 10 sites (6 ovary sites and 4 tubal sites), according to the classifications shown in Table 2 below.

Table 2
GRADES OF ADHESION SEVERITY

None (no adhesion)
Mild (a filmy avascular adhesion)
Severe (a dense organized cohesive vascular adhesion).

For each of the 10 anatomical sites (6 ovary sites and 4 tubal sites), the adhesion extent was assessed a numeric value assigned as shown in Table 3 below.

Table 3
GRADES OF ADHESION EXTENT

Extent	Numeric Value
None (no adhesion)	0
Localized (< 1/3 of the site covered)	1
Moderate (1/3 -2/3 of the site covered)	2
Extensive (> 2/3 of the site covered)	3

For each of the four regions (right ovary, right tube, left ovary, left tube), a single severity score and a single extent score was determined. A single severity score was assigned as the maximum of the anatomical site severities (*i.e.*, the clinically worst of none, mild, or severe). A single extent score was calculated by taking the average of the extent numeric values (0, 1, 2, or 3) from all sites making up the region (none, localized, moderate, extensive). This produced a single adhesion extent score as shown in Table 4 below.

Table 4
ADHESION EXTENT SCORES BASED ON AVERAGE OF
ANATOMICAL SITES MAKING UP EACH REGION

Average Extent Value	Adhesion Extent Score
0.00	None
0.33	Localized
0.50	Localized
0.67	Localized
1.00	Localized
1.33	Moderate
1.50	Moderate
1.67	Moderate
2.00	Moderate
2.33	Extensive
2.50	Extensive
2.67	Extensive
3.00	Extensive

Next, for each of the four regions (right ovary, right tube, left ovary, left tube) the severity and extent scores were converted to the AFS score as follows in Table 5:

Table 5
AFS SCORE BASED ON COMBINATION OF SEVERITY AND EXTENT
SCORES

Severity	Extent	Region score
None	None	0 (no adhesion)
Mild	Localized	1
Mild	Moderate	2
Mild	Extensive	4
Severe	Localized	4
Severe	Moderate	8
Severe	Extensive	16

Finally, the scores for the right tube and right ovary were added to obtain a single score for the right adnexa, and the scores for the left tube and left ovary were added to obtain a single score for the left adnexa. The AFS score (ranging from 0 to 32) was the minimum

of the right adnexa or left adnexa scores. If any structure was missing, the entire side was not scored and the AFS score was based only on the remaining side. Ranges of the AFS score were categorized into the following prognostic classifications for adnexal adhesions as shown in Table 6 below, reflecting AFS (1988):

Table 6
PROGNOSTIC CLASSIFICATION FOR ADNEXAL ADHESIONS

AFS Score Range	Prognostic Classification for Adnexal Adhesions
0-5	Minimal
6-10	Mild
11-20	Moderate
21-32	Severe